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Investigation into the Allylation Reactions of Aldehydes Promoted by the $CeCl_3\cdot 7H_2O$−NaI System as a Lewis Acid

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The Lewis acid promoted allylation of aldehydes has become an important carbon−carbon bond forming reaction in organic chemistry. In this context, we have developed an alternative over existing catalytic processes, wherein aldehydes are subject in acetonitrile to reaction of allylation with allyltributylstannane in the presence of 1.0 equiv of cerium(III) chloride heptahydrate ($CeCl_3\cdot 7H_2O$), an inexpensive and mild Lewis acid. The allylation has been accelerated by using an inorganic iodide as a cocatalyst, and various iodide salts were examined. The procedure must use allylstannane reagent instead of allylsilane reagent, desirable for environmental reasons, but high chemoselectivity was observed, and this is opposite the results obtained with other classical Lewis acids such as $TiCl_4$ and $Et_2O\cdot BF_3$.

Introduction

Lewis acids play a vital role in organic reactions, and in this respect, extensive efforts have been devoted to the exploration of new generations of these compounds.[1] Various kinds of Lewis acid promoted reactions were developed, and these reactions must be carried out under strictly anhydrous conditions. Even a small amount of water stops reactions using these species because the reagents immediately react with water rather than the substrates. For this reason new types of water-tolerant Lewis acids were developed.[2] In this regard, the lanthanide compounds have become attractive candidates for use as Lewis acid reagents in organic chemistry, and have found numerous applications as promoters.[3] The introduction of electronegative ligands such as triflates enhances the activity by increasing the Lewis acidity of the metal.[4] These catalysts offer several advantages including mild reaction conditions, cleaner reactions, shorter reaction times, high yield of the products, lower catalytic loading, and simple experimental and isolation procedures. However, these methods involve expensive reagents; thus, recently, cerium(III) chloride has become an attractive candidate for use as a Lewis acid in organic chemistry for its relative nontoxicity and ready availability at a low cost. In fact, after the pioneering works by Luche[5] and Imamoto[6] numerous reactions and methodologies employing cerium(III) derivatives as key components have been developed.[7] It has been observed that $CeCl_3$ plays a fundamental role in transferring a nucleophile moiety to electrophilic centers.[8]

In the course of our program aimed to develop new synthetic uses of $CeCl_3\cdot 7H_2O$[9] in reactions that need the presence of a Lewis acid activator, it was found that this salt acts as a promoter that facilitates the cleavage of the carbon−oxygen bond[10] and silicon−oxygen bond[11]

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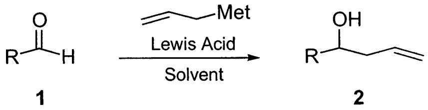
10.1021/jo035542o CCC: $27.50

SCHEME 1



under neutral conditions. In particular, we have observed that $CeCl_3$, being a hard Lewis acid,[12] is suitable to form a weak and labile iodide ion−Lewis acid complex.[10i] The nucleophile donor can enhance the electrophilicity of a Lewis acidic promoter, a concept masterfully developed by Denmark.[13] The $CeCl_3{\cdot}7H_2O$−NaI system appears, then, competitive and in several cases superior as a Lewis acid to preexisting protocols. To better evaluate the sodium iodide ability to enhance the activity of cerium trichloride as a Lewis acid, we have here investigated one of the most important carbon−carbon bond forming reactions in organic chemistry, the addition of allylmetal reagents to aldehydes.[14]

The allylation reaction represents one of the most useful methods for the preparation of homoallylic alcohols (Scheme 1), which are useful tools for the construction of complex molecules[15] and which can be easily converted to many important building blocks for natural product synthesis.[16] A number of such nucleophilic additions to carbonyl compounds have been developed, and in particular, the reactions with allylic metals bearing IUPAC periodic table group 14 elements in the presence of Lewis acid have been extensively studied because of their high reactivity and selectivity.[17] However, many of these reactions cannot be carried out in the presence of oxygen and moisture, which can decompose or deactivate the acid catalyst.[18] To circumvent these problems, new procedures have been developed for this conversion[19] using lanthanide triflates[20] and indium salts,[21] compounds less commonly employed for Lewis acid promoted carbon−carbon bond formation[22] as catalysts. Metal triflates are strongly acidic and highly expensive, whereas indium salts produce low Lewis acidity with respect to Ce(III) salts.[23] So the development of a neutral alternative such as our $CeCl_3{\cdot}7H_2O$−NaI combination would extend the scope of the important addition of various allylmetal reagents to carbonyl compounds.

Results and Discussion

We first examined the reaction of allyltrimethylsilane with aldehydes in the presence of $CeCl_3{\cdot}7H_2O$ and NaI, but no addition proceeded in acetonitrile. An attempt to increase the Lewis acidity of our system[24] by using this couple supported on silica gel[25] also failed to give the desired homoallylic adduct. Allylsilanes are generally more desirable than allylmetal reagents, particularly for environmental reasons. However, their lower reactivity[26] might not be sufficient to react with aldehydes in our reaction conditions; thus, other allylmetal reagents such

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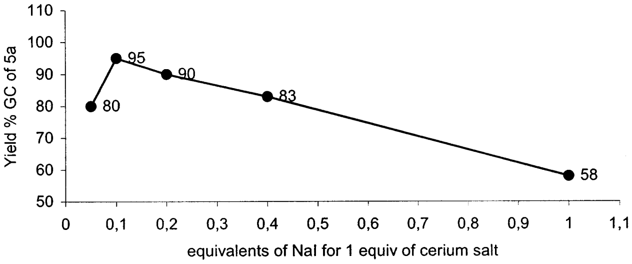
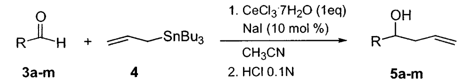


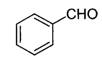
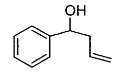
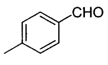
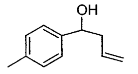
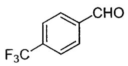
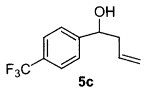
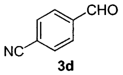
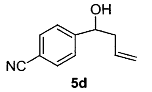
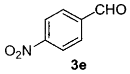
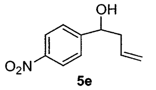
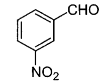
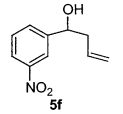
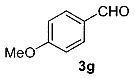
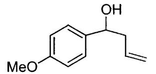
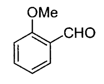
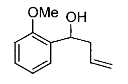
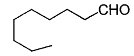
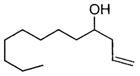
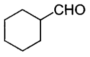
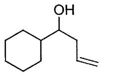
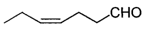
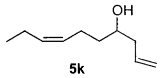
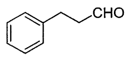
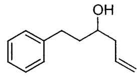
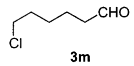
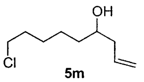
FIGURE 1. The amount of NaI influences the efficiency of the reaction.

as allylstannanes were added to the reaction mixture. Our attention was turned to using allyltributylstannane since it does not require rigorously dry conditions and an inert atmosphere, and in comparison with most metals it is relatively inexpensive and readily available.[27]

Benzaldehyde (**3a**) was examined as a model substrate as a ca. 0.1 M solution in acetonitrile containing 1.0 equiv of $CeCl_3.7H_2O$ and 1.0 equiv of NaI. After treatment with allyltributylstannane (**4**) the resulting heterogeneous reaction mixture was stirred and monitored by TLC and GC/MS. A homoallylic adduct (**5a**) was obtained in moderate yield (58%) after extractive workup and chromatography on a silica gel column. In optimizing the reaction conditions, we tested several combinations of NaI amounts. The results in Figure 1 indicate that the molecular percent of sodium iodide used is crucial, and a significantly lower yield of homoallyl alcohol **5a** was produced using more than 30 mol % NaI. Surprisingly, the addition of up to 20 mol % inhibits the reaction, and the tributyltin iodide (Bu_3SnI) identified by GC/MS indicates iodide ion binding to the tin metal with resulting decomposition of the allyl reagent.[28] Thus, the amount of NaI is decisive for this type of allylation, and 10 mol % has been the most appropriate. In the absence of NaI, the aldehyde **3a** reacts very slowly with the allylating agent and the yields are generally very low. For example, when **3a** was treated with allylmetal **4** and $CeCl_3{\cdot}7H_2O$ in acetonitrile, the corresponding homoallylic alcohol **5a** was isolated in only 28% yield after 5 days.[29] Likewise, when attempts to carry out allylation of **3a** with stannane **4** and NaI, in the absence of $CeCl_3{\cdot}7H_2O$, the almost quantitative recovery of aldehyde substrate was observed. However, addition of $CeCl_3{\cdot}7H_2O$ to this mixture resulted in the disappearance of the starting material.

TABLE 1. Cerium Trichloride−Sodium Iodide System Promoted Allylation of Aldehydes Using Allyltributylstannane



Entry	Aldehyde[a]	Time/h	Product[b]	Yield (%)[c]
1	 **3a**	27	 **5a**	95
2	 **3b**	36	 **5b**	80
3	 **3c**	24	 **5c**	92
4	 **3d**	21	 **5d**	93
5	 **3e**	19	 **5e**	87
6	 **3f**	18	 **5f**	95
7	 **3g**	27	 **5g**	78
8	 **3h**	30	 **5h**	83
9	 **3i**	22	 **5i**	91
10	 **3j**	20	 **5j**	85
11	 **3k**	25.5	 **5k**	93
12	 **3l**	20	 **5l**	75
13	 **3m**	20	 **5m**	16[d]

[a] All starting aldehydes were commercially available. [b] All products were identified by their IR, NMR, and GC/MS. [c] Yields of products isolated by column chromatography. [d] Yield by GC/MS analysis.

Encouraged by these results, we have carried out the allylation of a variety of aldehydes[30] to understand the scope and reactivity of our procedure, and the results are summarized in Table 1. The good-to-excellent yields strongly suggest that our $CeCl_3{\cdot}7H_2O{-}NaI$ system is an efficient Lewis acid promoter for the allylation of aldehydes. The reaction proved to be general and could be applied to a broad range of aldehydes. Specifically, the reaction proceeds smoothly under very mild conditions at room temperature.[31] There is no need to exclude moisture or oxygen from the reaction system, and the

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[27] (a) Chan, T. H.; Yang, Y.; Li, C. J. *J. Org. Chem.* **1999**, *64*, 4452.4455. (b) Chataiguer, I.; Piarulli, L.; Gennari, C. *Tetrahedron Lett.* **1999**, *40*, 3633−3634. (c) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063-2192.

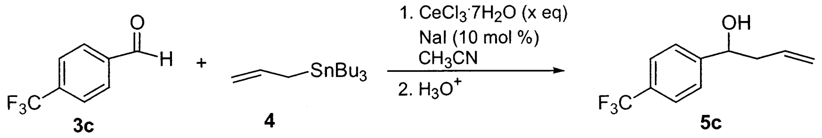
[28] Light, J. P.; Ridenour, M.; Beard, L.; Herhberger, J. W. *J. Organomet. Chem.* **1987**, *326*, 17−24.

[29] No reaction took place in the absence of $CeCl_3{\cdot}7H_2O$.

[30] Unfortunately, the desired allylation did not proceed well from α,β-unsaturated carbonyl compounds (Table, entry 13).

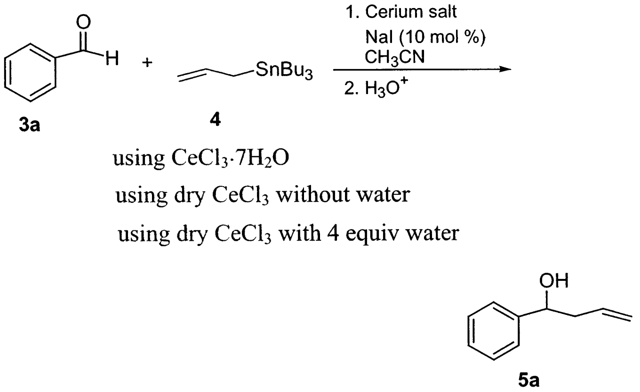
[31] See the Supporting Information (SI) for details.

SCHEME 2



Time/h	8	16	24
x = 0.7 eq. / yield % of **5c**	56	62	77
x = 1.0 eq. / yield % of **5c**	66	82	92
x = 1.3 eq. / yield % of **5c**	76	78	83

SCHEME 3



using $CeCl_3 \cdot 7H_2O$	92% conv.
using dry $CeCl_3$ without water	10% conv.
using dry $CeCl_3$ with 4 equiv water	90% conv.

removal of any excess of allyltributylstannane and other tin byproducts by treatment with 10 mol % KF and rapid filtration through silica gel[32] clearly demonstrate these advantages. It should be noted that the complex $CeCl_3 \cdot 7H_2O-NaI$ system promotes the allylation of both aromatic and aliphatic aldehydes, giving excellent yields of product **5** in a short period. Enolizable aldehydes also produce the corresponding homoallylic alcohol in good yields (entries 9, 10, and 12). Furthermore, the treatment of aldehyde **3k** with allylstannane **4** in our reaction conditions gave only the homoallylic alcohol **5k** without a trace of *Z*−*E* isomerization of the double bond, and no oxyceriation[11a] of the carbon−carbon double bond is involved. Thus, a simple Brønsted acid (HX) catalyzed mechanism cannot explain all these observations, since it is known that allyltributylstannanes do not react with carbonyl compounds in the presence of halogen acids.[33] Only when the above-described methodology was applied to aldehyde **3m**,[34] a low yield of adduct **5m**, as identified by GC/MS, was obtained with formation of a mixture of unidentifiable products, and this might be attributed to nucleophilic substitution by iodide ion (Table 1, entry 13).

It is interesting to note that a stoichiometric amount of $CeCl_3 \cdot 7H_2O$ is required for high efficiency, whereas an excess of cerium salt leads to lower yields (Scheme 2), and GC/MS analysis of the mixture reaction shows the decomposition of allylstannane **4** with formation of tributyltin chloride (Bu_3SnCl). We have also examined the possibility of $CeCl_3 \cdot 7H_2O$ functioning catalytically or at least in less than stoichiometric amounts. But the best results were obtained with an equimolar ratio of cerium trichloride and aldehydes. To improve the efficiency of the promoter system, we have examined different ratios among the aldehydes, allyltributylstannane, cerium salt, and the iodide. The best results were found (Table 1) when the ratio [aldehyde]:[$CH_2{=}CHCH_2SnBu_3$]:[$CeCl_3 \cdot 7H_2O$]:[NaI] was 1:1:1:0.1. Interestingly, since an amount of $CeCl_3$ equivalent to that of the aldehydes gives the best result in these allylations, we believe that an *n*:*n* complex[35] of substrate and $CeCl_3$ would be the most effective species.

Having established what appeared to be the optimal conditions, we switched our attention to the water of crystallization of the salt. Water (from $CeCl_3 \cdot 7H_2O$) is an important component of the reaction system and does not decrease the yield of homoallylic alcohol, as a consequence of a possible competitive aldehyde dimer formation. For our methodology, in fact, the cerium trichloride has been utilized as a heptahydrate complex. When anhydrous cerium(III) chloride salt[36] was employed in dry solvent, the rate dropped dramatically (Scheme 3). However, by adding 1 equiv of water to the dry reaction mixture, we have obtained the same reactivity as with the cerium salt heptahydrate. In particular, with <1 equiv of water, decreased activity was observed, while with 1, 4, 7, and 10 equiv of water, essentially identical results were obtained. It is also worth noting that the reaction of **3a** with allylmetal reagent **4** in the presence of our $CeCl_3 \cdot 7H_2O-NaI$ system was significantly accelerated by exposing the stirring mixture to the atmosphere. Comparing the rate of allylation of benzaldehyde when exposed to air (through a $MgSO_4$ drying tube) to the rate with the use of water added and acetonitrile as solvent demonstrated that water, and not oxygen, accelerates the reaction. The role of the water is not clearly understood at this time. The reaction behaves empirically as though an inactive complex is generated in the absence of water. Thus, without conclusive data, we postulate that the

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[32] Davies, A. G. *Organotin Chemistry*; Wiley-VCH: Weinheim, Germany, 1997.

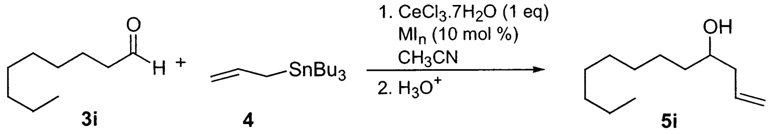
[33] Yanagisawa, A.; Morodome, M.; Nakashima, H.; Yamamoto, H. *Synlett* **1997**, 1309−1311.

[34] Marcantoni, E.; Mecozzi, T.; Petrini, M. *J. Org. Chem.* **2002**, *67*, 2989−2994.

[35] Analogously to Yamamoto's work (Nakamura, H.; Ishihara, K.; Yamamoto, H. *J. Org. Chem.* **2002**, *67*, 5124−5137), we have no evidence that the complex consists of one aldehyde molecule and one $CeCl_3$ molecule. There is a possibility that a 2:2, 4:4, or *n*:*n* complex exists.

[36] Imamoto, T.; Takeda, N. *Org. Synth.* **1998**, *76*, 228−238.

SCHEME 4



MI_n	CuI	ZnI_2	CdI_2	LiI	KI	CsI	NaI
Yield % of **5i**	0	68	62	3	76	3	91

cerium center may require ligation by 1 or more equiv of water for generating fully active species.[37] It is known,[38] in fact, that very probably the water preferentially coordinates the cerium chloride, promoting the dissociation of chloride anion to form a more active Lewis acid species by the reaction

$$CeCl_3(\text{solvent})_m + H_2O \rightleftharpoons [CeCl_{3-n}(\text{solvent})_m(H_2O)]^+ + Cl^- \quad (1)$$

The effect of solvent was then investigated. Previous works by this group on the organic transformations promoted by the $CeCl_3 \cdot 7H_2O-NaI$ combination suggested that acetonitrile is likely to be the solvent of choice for this allylation.[11b] Other solvents were examined, and solvents such as CH_2Cl_2, THF, DMF, or nitromethane were not useful for this reaction. Similarly, without organic solvent the allylation of aldehyde **3a** was not successful. Rather, the reaction concentration also proved to be an important factor in obtaining the allylation products in good yields. A concentration of ca. 0.1 M with respect to the aldehydes is optimal. Poor yields were obtained at concentrations greater than 0.5 M.

Next, we surveyed the acceleration effect caused by addition of sodium iodide to $CeCl_3$. This effect might be rationalized by a halogen exchange reaction[39] that leads to more soluble species (eq 2).

$$CeCl_3 + n\text{NaI} \xrightarrow[n\,=\,1-3]{} CeCl_{3-n}I_n + n\text{NaCl} \quad (2)$$

However, hydrated CeI_3 alone shows an activity only slightly superior to that of $CeCl_3 \cdot 7H_2O$, but significatively lower than that of the $CeCl_3 \cdot 7H_2O-NaI$ combination. Moreover, the system $CeCl_3 \cdot 7H_2O-3NaI$ is less efficient than $CeCl_3 \cdot 7H_2O-0.2NaI$. Then, another process might be plausible. For this reason various inorganic iodides were examined in the model reaction of nonal (**3i**) with **4** promoted by the Lewis acidity of cerium(III) chloride. Data for the yields vs different iodides are summarized in Scheme 4. Among them, some iodides, other than NaI, have displayed some activity, but others such as CuI and LiI have been revealed as ineffective.

Certainly, it is premature to speculate on the exact mechanism provided by the anion iodide, but we have obtained some evidence that the reaction is promoted by the solid $CeCl_3 \cdot 7H_2O-NaI$ system. In fact, $CeCl_3 \cdot 7H_2O$, which is poorly soluble in acetonitrile (ca. 0.03 M),[40] and NaI were stirred in acetonitrile for 24 h at room temperature; afterward the mixture was filtered. To the filtrate was added benzaldehyde **3a** and allylmetal reagent **4**, and the solution was stirred under the same conditions as in Table 1, entry 1. The yield of the desired homoallylic alcohol was only 6%, and apparently, the allylation reaction in the homogeneous phase is very slow. Thus, we believe that the disaggregation of the crystal lattice of $CeCl_3$ by NaI (similarly by ZnI_2, CdI_2, and KI) might lead to a notable increase in the Lewis acidity of the cerium available at the particle surface. Therefore, the catalytic activity of inorganic iodide salts (MI_n) seems directly dependent on their particle size, and not on the nature of the metal M. In fact, the $CeCl_3 \cdot 7H_2O-ZnI_2$ combination, which gives a fine powder, shows an activity similar to that of the $CeCl_3 \cdot 7H_2O-NaI$ system, and both are more active systems than $CeCl_3 \cdot 7H_2O-CuI$, which produces a coarser powder. All this evidence strongly suggests that the activity of the $CeCl_3 \cdot 7H_2O-NaI$ system is mainly exerted in the heterogeneous phase. Although there are a striking number of chemical physics tools available,[41] unfortunately, all the effort of structural characterization of the complex was unsuccessful, since it was impossible to obtain reliable X-ray information. Efforts are under way in these laboratories to explore the role of this Lewis acid promoter for several organic transformations. Moreover, we decided to investigate the use of iodine on the allylation of aldehydes.[22a] We have found that when a mixture of aldehyde **3a** (1 equiv) and allylating reagent **4** (1 equiv) is treated with $CeCl_3 \cdot 7H_2O$ (1 equiv) and a catalytic amount of elemental iodine (10 mol %), the reaction is not more efficient than treatment with $CeCl_3 \cdot 7H_2O$ alone. This result might indicate that in our reaction conditions the oxidization of iodide ion to iodine does not happen.

To provide a firm foundation for an understanding of how our $CeCl_3 \cdot 7H_2O-NaI$ system promotes the addition of allyltributylstannane to aldehydes, it is essential to establish how this reagent system interacts with the two reaction components. For this we decided to see if the allylstannane **4** would undergo transmetalation[42] when exposed to $CeCl_3$ and determine the mode of complexation

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(37) For the coordination chemistry of lanthanide halides, see: (a) Evans, W. J.; Feldman, J. D.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 4581−4584. (b) Evans, W. J.; Shreeve, J. L.; Ziller, J. W.; Doedens, R. J. *Inorg. Chem.* **1995**, *34*, 576−585.

(38) Glinski, J.; Keller, B.; Legendziewicz, J.; Samela, S. *J. Mol. Struct.* **2001**, 59−66.

(39) (a) Fukuzawa, S.; Tsuruta, T.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1473−1477. (b) Fukuzawa, S.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Chem. Commun.* **1985**, 777−778.

(40) *The Merck Index*, 12th ed.; Merck & Co., Inc.: Whitehouse Station, NJ, 1996; p 332.

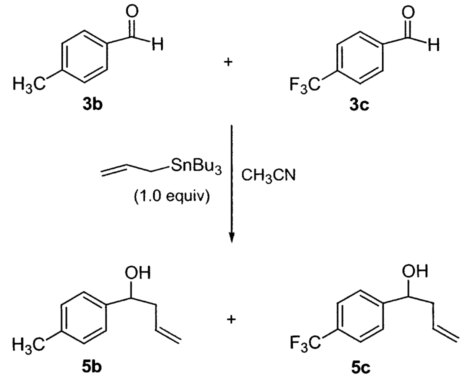
(41) Copéret, C.; Thivolle-Cazat, J.; Basset, J.-M. In *Fine Chemicals through Heterogeneous Catalysis*; Sheldon, R. A., van Bekkum, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001; p 553.

(42) (a) Denmark, S. E.; Almstead, N. G. *Tetrahedron* **1992**, *48*, 5565−5578. (b) Keck, G. E.; Castellino, S.; Andrus, M. B. In *Selectivities in Lewis Acid Promoted Reactions*; Schinzer, D., Ed.; Kluwer Academic Publishers: Dodrecht, The Netherlands, 1989; pp 73−105. (c) Denmark, S. E.; Weber, E. J.; Wilson, T. M. *Tetrahedron* **1989**, *111*, 8136−8141.

of cerium salt with aldehydes. The process was studied using allyltributylstannane in a 0.1 M solution of $CDCl_3$. The addition of $CeCl_3$ to this solution at −78 °C resulted in ^{13}C NMR signals very broad, and not readily identifiable species could be discerned from the spectra, due, very probably, to the presence of paramagnetic Ce(III) species.[8b,43] However, signals for the starting material remained, and no change in the ^{13}C NMR spectra was observed when the $CeCl_3$ was added at −78 °C, the mixture was placed in the spectrometer, and spectra were observed at 30 °C intervals (approximatevely every 1/2 hour). Even after 1 day at room temperature there was no transmetalation of the allyltributylstannane. Therefore, we believe that $CeCl_3$ promoted reactions of allylstannanes with aldehydes do not involve allylchlorocerium species originated by transmetalation. Certainly, apart from this transmetalation reaction, allylcerium(III) species might be generated by oxidative addition of cerium.[44] The reaction of allyl bromide with cerium metal,[45] benzaldehyde **3a**, and sodium iodide, in typical Hiyama−Nozaki conditions,[46] did not show, however, the expected homoallyl alcohol **5a**. We have not detected traces of **5a** or oxidation products derived from this adduct[47] by GC/MS analysis of the crude reaction mixture after stirring in acetonitrile for 24 h. The participation of an allylcerium species can be ruled out even by the fact that lower yields of homoallyl alcohol adducts are obtained when 1.3 equiv of $CeCl_3{\cdot}7H_2O$ are used (Scheme 2). In these conditions, the excess of cerium salt promotes the decomposition of **4** to afford Bu_3SnCl, as identified by GC/MS. Given these studies we can suppose that in our allylation of aldehydes promoted by the $CeCl_3{\cdot}7H_2O$−NaI system the reaction does not proceed via transmetalation to yield a reactive allylmetal halide, which then reacts with the carbonyl compound. We presume that the allylstannanes can act as allyl anion equivalents, and the reaction may proceed via addition to a Lewis acid−carbonyl compound complex. For this we have tried to study the complexation of aldehyde **3a** with $CeCl_3$ by ^{13}C NMR spectroscopy. In this case, nevertheless, the ^{13}C NMR signals observed were very broad, and no identifiable species could be discerned from the spectra.

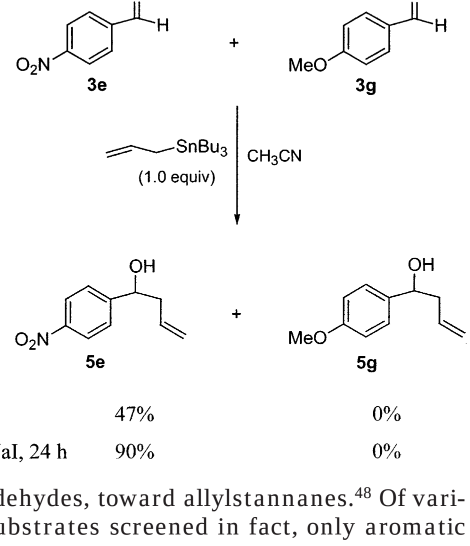
Although the mechanism remains unclear, the procedure exhibits high chemoselectivity toward aldehydes in the presence of ketones when the allylation is conducted in a binary substrate system, *p*-tolualdehyde and propiophenone; only aldehydes were allylated to the extent of 74%, whereas the ketone was not allylated at the same time. This is due to the lower reactivity of ketones, compared to aldehydes, toward allylstannanes.[48] Of various carbonyl substrates screened in fact, only aromatic and aliphatic aldehydes were reactive substrates. This chemoselectivity was further evaluated by crossover experiments (Schemes 5 and 6) of **4** with substituted aryl aldehydes, respectively. The reaction of a 1:1 mixture of **3b** (1 equiv) and **3c** (1 equiv) gave a small amount (7% yield) of **5c** along with the recovered **3c** (84% yield) and **3b** (>99% yield). On the other hand, the $CeCl_3{\cdot}7H_2O$−NaI system promoted allylation of a 1:1 mixture of **3b** and **3c** under $Bu_3SnCH_2CH{=}CH_2$ (1 equiv) without Lewis acid promoter gave after 24 h at room temperature in the same reaction conditions as above **5c** in 86% yield along with recovered **3b** (99% yield). High chemoselectivity was also observed when a 1:1 mixture of **3e** (1 equiv) and **3g** (1 equiv) was treated with 1 equiv of **4** under the same reaction conditions as above. The allylation product **5e** was obtained in 47% and 90% yield, respectively, together with **3g**, which was recovered quantitatively in both cases. This remarkable chemoselectivity suggests the following interesting electronic

SCHEME 5



	5b	5c
r. t., 24 h	0%	7%
r. t., $CeCl_3{\cdot}7H_2O$-NaI, 24 h	0%	86%

SCHEME 6



	5e	5g
r. t., 24 h	47%	0%
r. t., $CeCl_3{\cdot}7H_2O$-NaI, 24 h	90%	0%

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(43) (a) The paramagnetism of Ce(III) precluded obtaining useful ^1H NMR information: Hubert-Pfalzgraf, L. G.; Machado, L. *Polyhedron* **1996**, *15*, 545−549. Stecher, H. A., Seu, A.; Rheingold, A. L. *Inorg. Chem.* **1989**, *28*, 3280−3282. See also ref 8b. (b) An attempt of studying this process in more expensive acetonitrile-*d*$_3$ than $CDCl_3$ afforded more complicated results.

(44) (a) Lee, A. S.-Y.; Wu, C.-W. *Tetrahedron* **1999**, *55*, 12531−12542. (b) Guo, B.-S.; Doubleday: W.; Cohen, T. *J. Am. Chem. Soc.* **1987**, *109*, 4710−4711.

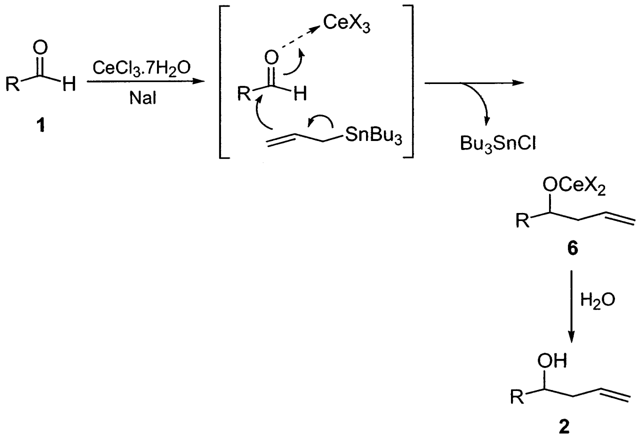
(45) Imamoto, T.; Kusumoto, T. Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904−3912.

(46) (a) Hiyama, T.; Kimura, K.; Nozak, H.; Okude, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 561−567. (b) Okude, Y.; Hirano, S.; Hiyama, T., Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179−3180.

(47) (a) Schrekker, H. S.; de Bolster, m. W. G.; Orru, R. V. A.; Wessjoham, L. A. *J. Org. Chem.* **2002**, *67*, 1975−1981. (b) Hudlick, M. *Oxidations in Organic Chemistry*; Americam Chemical Society: Washington, DC, 1990.

(48) For examples of allylation reactions of ketones, see: (a) Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483−485. (b) Hanawa, H.; Kii, S.; Maruoka, K. *Adv. Synth. Catal.* **2001**, *343*, 57−61. (c) Hamasaki, R.; Chounan, Y.; Horino, H.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 9883−9887. (d) Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett.* **1999**, *1*, 1061−1064.

SCHEME 7



effects: (a) aryl aldehydes with an electron-withdrawing substituent (i.e., NO_2, CF_3) react much faster than benzaldehyde and (b) an electron-donating substituent (i.e., CH_3, OCH_3) deactivated aryl aldehyde remarkably. Seemingly, this reactivity of aldehydes is principally dependent on the inherent electrophilicity of carbonyl, not on the electron density of the formyl oxygen.[49] Moreover, the rate observed for *p*-nitrobenzaldehyde is likely to originate from its electronic effect rather than the interfering coordination by the NO_2 group.

The high coordinating ability of the cerium(III) toward oxygen atoms of the carbonyl moiety[3b,50] is presumably responsible for the effective activation of aldehydic carbonyl independently of the electronic effect for aryl aldehyde substrate. These results suggest us that the relative reactivity of aldehydes in the $CeCl_3{\cdot}7H_2O-NaI$ promoted process is determined almost solely by the electrophilicity of aldehydes themselves, not by the coordinating ability of aldehydes to the cerium lanthanoid. These findings strongly support a pathway for the reaction (Scheme 7) where we believe that the activation of the aldehydes probably occurs via formation of an oxonium salt with cerium chloride for its oxophilic character. Then, the rapid protonation of cerium alkoxide **6** by reaction with water generates the target homoallylic alcohol **2**. The alkoxides of lanthanides are notoriously Brønsted basic, and almost instantaneous reaction with H_2O is generally observed, yielding highly insoluble lanthanide hydroxide species.[51] In addition, this allylation reaction needs a stoichiometric amount of cerium trichloride because of the above strong interaction with the oxygen function.[52]

Finally, it is worth noting that the activity of our $CeCl_3{\cdot}7H_2O-NaI$ system in the allylation reactions of aldehydes is opposite to some extent that of strong Lewis acids, i.e., $TiCl_4$ and $Et_2O{\cdot}BF_3$, which selectively activate aryl aldehydes with an electron-donating substituent. It should be noted that, in the course of our program to develop new synthetic Lewis acid mediated transformations, we have already found opposite effects between $CeCl_3$ and $TiCl_4$.[8b,53,54] This study, thus, represents another example of how cerium(III) salts promote an organic transformation with a chemoselectivity that is reversed compared to that of the classical Lewis acid mediated reactions.

At the end of these investigations it is clear that the allylation reactions of aldehydes by allylstannanes are particularly effective in the presence of a Lewis acid and, most of all, the chemoselectivity depends on the nature of the metal atom of the Lewis acid. With certain aldehydes we have found that the $CeCl_3{\cdot}7H_2O-NaI$ system is instrumental in determining an opposite chemoselective outcome with respect to that of $TiCl_4$ or BF_3. In summary, the study has shown how our allylation method may be an alternative to the previously reported methods, and the tolerance of water and air stability of the $CeCl_3{\cdot}7H_2O-NaI$ system offers distinct advantages over the more common Lewis acids. Further work is in progress in our laboratories to study the regio- and stereoselectivity, and to attempt the preparation of units which might function as important synthetic targets in organic chemistry. Moreover, we are currently expanding the study of this allylation reaction of aldehydes in using other allylmetal reagents that are desirable for environmental reasons.

Experimental Section[55]

The compounds 1-phenyl-3-buten-1-ol (**5a**),[56] 1-(4-methylphenyl)-3-buten-1-ol (**5b**),[57] 1-[4-(trifluoromethyl)phenyl]-3-buten-1-ol (**5c**),[58] 4-(1-hydroxy-3-butenyl)benzonitrile (**5d**),[59] 1-(4-nitrophenyl)-3-buten-1-ol (**5e**),[59] 1-(4-methoxyphenyl)-3-buten-1-ol (**5g**),[60] 1-(2-methoxyphenyl)-3-buten-1-ol (**5h**),[61] 1-dodecen-4-ol (**5i**),[56] 1-cyclohexyl-3-buten-1-ol (**5j**),[60] 1-phenyl-5-hexen-3-ol (**5l**),[62] and (1*E*)-1-phenyl-1,5-hexadien-3-ol (**5m**)[63] are all known, and their structures are consistent with their published physical data.

General Procedure for the Allylation (5a−m). To a suspension of $CeCl_3{\cdot}7H_2O$ (1.0 mmol) and NaI (0.1 mmol) in acetonitrile (12 mL) were added successively aldehydes **3a−m** (1.0 mmol) and allyltributylstannane (**4**) (1.1 mmol) at room temperature. After being stirred at that temperature for the required time, the reaction mixture was quenched with 0.1 N HCl solution. The aqueous layer was extracted with diethyl

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[49] For a mechanistic discussion, see: Asao, N.; Asano, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 3206−3208 and references therein.

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ether, and the combined organic layers were stirred for 1 h with 10% KF in H_2O (10 mL). The organic phase was separated, washed with brine, dried with Na_2SO_4, and concentrated at reduced pressure to furnish the crude product, which was purified by silica gel chromatography (hexanes: EtOAc).

Data for 1-(3-nitrophenyl)-3-buten-1-ol (5f): yellow oil (yield 95%); IR (neat, cm^{-1}) 3400, 3078, 1641, 1529, 1350; ^1H NMR δ 2.50−2.65 (m, 3H), 4.82−4.90 (m, 1H), 5.12−5.26 (m, 2H), 5.70−5.91 (m, 1H), 7.40−7.52 (m, 1H), 7.75 (d, 1H, $J = 1.27$ Hz), 8.13 (d, 1H, $J = 1.10$ Hz), 8.23 (s, 1H); ^{13}C NMR δ 40.0, 74.5, 113.6, 123.6, 124.0, 130.2, 134.6, 136.2, 139.0, 148.2; EI-MS *m/z* 193 [M^+], 152 (100), 105, 77, 65, 51, 41. Anal. Calcd for $C_{10}H_{10}NO_3$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.45; H, 5.27; N, 7.32.

Data for (7*Z*)-1,7-decadien-4-ol (5k): oil (yield 93%); IR (neat, cm^{-1}) 3368, 3077, 1640; ^1H NMR δ 0.93 (t, 3H, $J = 7.32$ Hz), 1.45−1.53 (m, 2H), 1.71 (bs, 1H, OH), 1.98−2.10 (m, 5H), 2.13−2.17 (m, 1H), 3.57−3.69 (m, 1H), 5.06−5.13 (m, 2H), 5.35 (dt, 2H, $J = 8.55$ and 7.34 Hz), 5.73−5.85 (m, 1H); ^{13}C NMR δ 14.0, 15.8, 22.0, 28.6, 39.2, 69.9, 113.2, 126.8, 130.6, 132.6; EI-MS *m/z* 154 [M^+], 136, 113, 95 (100), 69, 55, 41. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.85; H, 11.29.

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Supporting Information Available: General methods; experimental procedure and characterization for compounds **5f** and **5k**. This material is available free of charge via the Internet at http://pubs.acs.org.

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